MIT technology insider
FROM THE EDITORS OF TECHNOLOGY REVIEW

CONTENTS | 8.03

KEY

	FUNDING
$	UNDER $2 MILLION
$$	$2 MIL.-$10 MIL.
$$$	$10 MILLION PLUS
	PATENT STRENGTH
🗋	NO CORE PATENTS
🗋🗋	CORE PROTECTION
🗋🗋🗋	DOMINANT POSITION
	TIME TO MARKET
🕒	LESS THAN 1 YEAR
🕒🕒	1-3 YEARS
🕒🕒🕒	MORE THAN 3 YEARS

AN MIT ENTERPRISE TECHNOLOGY REVIEW

SPINOFF SPOTLIGHT

Fountain of Youth

ELIXIR IS DEVELOPING DRUGS THAT TARGET THE PROTEINS THAT CAUSE AGING

Want to live forever? That's probably not possible, but everyone seeks to live a longer and healthier life. That's why in the early 1990s, Lenny Guarente, a professor of biology at MIT, began doing research on the molecular biochemistry of aging. By isolating the genes that control aging and understanding the functions of the proteins encoded by those genes, Guarente believes he has found a fundamentally new way to fight diseases associated with aging, like heart disease, cancer, and diabetes. Elixir Pharmaceuticals, the company he cofounded on the basis of these findings, is now taking his research to the next level, developing drug compounds that affect the activity of proteins encoded by the so-called longevity genes.

The concept: instead of trying to put out individual fires—that is, targeting specific diseases of aging—Elixir seeks to fix the fuel leak that makes the atmosphere so combustible. "For most diseases that we care about, age is by far the major predisposing factor," says Ed Cannon, Elixir's chief executive. "If we understand the genes and pathways that regulate aging, we will gain new insights into all these diseases, and novel targets for disease intervention. We get more shots on goal."

The technology is rooted in the blood, sweat, and tears of hard-core laboratory research. In the late 1990s, Guarente and his colleagues discovered that a single gene called Sir2 regulates aging in both yeast and worms. ("Sir" stands for silent information regulator.) What's remarkable about this discovery is that these species diverged a billion years ago; that means the gene is universal, says Guarente, so it's in humans too. The researchers figured out how the protein encoded by the Sir2 gene regulates the aging process; they could thus alter its activity biochemically to change the life spans of simple organisms. In a striking proof of concept, Guarente's team produced genetically modified yeast that lived twice as long as the ordinary kind. Now Guarente and his company are testing links between the corresponding genes in mammals and resistance to diseases.

This approach, however, flies in the face of conventional drug development. Pharmaceutical companies like Geron, Genzyme, and LifeSpan Biosciences tend to focus on treating particular diseases or targeting the cellular symptoms of aging. But in the past five years, there has been a "renaissance in aging research," says Gary Ruvkun, a professor of genetics at Harvard Medical School and Massachusetts General Hospital in Boston. The basic science behind Elixir, he says, is "profound and interesting." But how just a few genes can control the entire aging process is by no means well understood, and some contest the very premise. Even a proponent like Ruvkun calls Elixir's approach "audacious" and predicts it will take decades to have any clinical impact.

Still, Elixir has a strong dose of scientific and business credibility. Guarente, along with the well-known molecular biologist Cynthia Kenyon at the University of California, San Francisco, and the biotech entrepreneur Cindy Bayley, who had previously founded Adolor and deCODE Genetics, incorporated the company in 1999. After raising $8.5 million in seed funding from Arch Venture Partners, Oxford Bioscience Partners, and Perennial Ventures (formerly Tredegar Investments) in 2000, the company began to solidify its management team. In April 2001, Elixir's founders brought aboard Cannon, a former immunologist at Brandeis University

CONTINUED ON PAGE 2

AT A GLANCE

NAME
Elixir Pharmaceuticals

CONTACT
Phone: 617-995-7000
www.elixirpharm.com

PRODUCTS
Developing drugs that target proteins that cause aging

INVESTORS
Arch Venture Partners, MPM Capital, Oxford Bioscience Partners, and Perennial Ventures

and the University of Massachusetts Medical School and a veteran executive of the biotechnology companies Protein Engineering, Dyax, and Hygeia Sciences.

Elixir's scientists have identified genes in mice and rats that regulate what cells do when they are damaged or put under stress. Roughly speaking, such a cell will either repair itself or kill itself. To treat heart disease, a drug could activate a gene that makes cells fight harder to survive; a different drug could deactivate another gene to make cancerous cells die off before tumors spread. With this approach, the scientists hope to produce a pill that can increase human life spans by 20 to 30 percent. What's more, say Guarente and Cannon, it will come within our lifetimes.

A visit to Elixir's offices in Kendall Square finds scientists typing at workstations and rushing between cold rooms, lab benches, and a myriad of bobbing and weaving platforms for mixing chemicals. The company is in the process of expanding. In February, Elixir merged with Cambridge, MA-based Centagenetix, keeping the name Elixir. Led by Thomas Perls, the director of the New England Centenarian Study at the Boston Medical Center and an associate professor of medicine at Boston University Medical School, Centagenetix scientists and executives brought to the table their expertise in analyzing genomic information from families with a large number of members who lived to be 100 years old. Their database of medical histories and DNA samples provides a way to map the animal experiments onto human genetics.

In the last year, Elixir has grown to 35 employees, which is encouraging; but its workforce is still too small to sort through thousands of chemical compounds each month and test their ability to react with enzymes and other proteins. So the company outsources some of this work to corporate partners such as Evotec-OAI, located both in Hamburg, Germany, and Oxford, England, whose hundreds of full-time chemists supply the R&D horsepower to develop useful new compounds.

Although it is years from having a product to sell—and despite a difficult investment climate—Elixir has no immediate financial concerns. This year's latest round of fundraising (Series B), which includes new investors like MPM Capital, has netted Elixir $22 million; another $15 million is expected by the round's close this fall. The money should last the company about three years, says Cannon.

In the next year or so, Elixir plans to enter into a partnership with a large pharmaceutical company—on the scale of Merck or Bristol-Myers Squibb—to begin developing drugs to treat neurodegenerative diseases and cancer. For diseases like Huntington's and amyotrophic lateral sclerosis (Lou Gehrig's Disease), which present smaller drug markets, Elixir may put out its own products, says Cannon. But it will take time—probably eight to 10 years—to get U.S. Food and Drug Administration approval and run clinical trials.

In the short term, the main challenges are technical: how to translate effective drug compounds from test tubes to living animals. It's one thing to demonstrate effects in yeast and worms, but quite another to "get the complexities right" in mammals, says Guarente. That's what will convince the big drug companies to pick up the ball—and the payoffs would be enormous.

Amidst the speculation, though, one thing is constant. "Even as financial markets have gone down, the science keeps going up," says Cannon. "At the end of the day, that's what will pay off." If Elixir is ultimately successful, our life spans will be going up too.

MIT technology insider
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- MIT researchers address issues of energy efficiency

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- Environmental chemicals may not cause cancerous mutations, biologist says

  web.mit.edu/newsoffice/nr/2003/thilly.html

- MULTIMEDIA LINK: Whitehead's Rudolf Jaenisch dispels misconceptions about stem cell research and cloning

  mitworld.mit.edu/video/138/

Advances against Schizophrenia

Researchers at the Picower Center for Learning and Memory have discovered a gene variation in mice that could cause schizophrenia, and in a separate collaboration with scientists at New York's Rockefeller University, they found a human gene associated with the disease. The work could lead to the first gene-targeting drug for schizophrenia.

The first study, led by Nobel laureate Susumu Tonegawa, involved breeding genetically altered mice that lacked a key brain protein, calcineurin. The absence of this protein was previously thought to result only in short-term memory loss. The researchers found, however, that calcineurin-deficient mice displayed symptoms of schizophrenia, including attention deficits and abnormal social behavior.

In additional tests, the MIT and Rockefeller scientists checked DNA samples from schizophrenia patients and their relatives for the calcineurin gene. These tests revealed links between schizophrenia and a particular calcineurin gene—one similar to the gene in the mice study. "The combination of evidence from the genetically altered mice, along with the human gene studies, gives a strong indication of calcineurin's link with schizophrenia," says MIT research scientist David Gerber.

The research was reported in the July 22 issue of *Proceedings of the National Academy of Sciences.*

Manipulating Light

MIT physicists have discovered a new method for controlling light, which may lead to applications in telecommunications.

Physics postdoctoral associate Evan Reed and his colleagues simulated the interactions of shock waves and light inside a photonic crystal. They found that a shocked crystal could change the frequency of a light signal—making blue light turn red, for example. It could also trap light for a controlled period of time. The simulations showed that shock waves sent through the crystal compressed parts of its structure, trapping light. The light then bounced back and forth until it escaped with a different frequency.

Reed says this technique can be used to control light signals of any intensity and could therefore prove a much better alternative to current experimental methods of frequency control, which require high-power light sources. In addition, unlike other approaches, the technique makes it possible to narrow a light signal's bandwidth without any energy loss.

These results may make it possible for photonics equipment to replace electronics in telecommunications networks. "It's an all-optical approach to frequency conversion," Reed says, "so it should be very fast compared to current approaches that involve electronics."

Time-Sensitive Mapping

Media Lab Europe researcher Brendan Donovan has developed software that gives maps a sense of time. Called Amble Time, it lets a user enter her walking pace, final destination, and desired arrival time. Then a bubble on a map indicates the area within which the user can roam and still make it to her destination on time. When the software is running on a GPS-enabled device, the bubble will move along with the user as she walks.

Donovan thinks the software would be particularly useful for tourists on tight schedules, as it would allow them to enjoy sightseeing without constantly checking their watches and poring over maps. A prototype runs on a desktop computer and uses a map of Dublin. Donovan next plans to create a version that will work with handhelds and draw on data from any type of map that users may want to consult.

Treatment for Chronic Lung Disease

An MIT-affiliated researcher has developed a new method to increase the amount of oxygen in the bloodstream. His approach could improve the quality of life of people with chronic lung disease, which slowly destroys the lungs' ability to replenish oxygen in blood. It could also decrease the mortality rate of those awaiting lung transplants by serving as a transition therapy.

Developed by Richard Gilbert, a physician allied with the Department of Mechanical Engineering, the technique extracts oxygen from the water within a patient's blood cells. That oxygen then binds to the hemoglobin in the cells, raising the oxygen level in the blood until it matches that produced by healthy lungs.

The patient's blood is removed from the body (as in kidney dialysis) and passed over a piece of glass coated with a thin skin of titanium oxide. Ultraviolet light energizes the titanium, which draws electrons from the water, freeing oxygen molecules. Then the oxygenated blood is pumped back into the body.

There is no explicit treatment for chronic lung disease, Gilbert says, so "most of the time, people just deteriorate and die a terrible death." He believes his system could allow people afflicted with the disease to lead normal lives. The first device to employ this system will be a portable one about the size of a breadbox. Gilbert estimates it will be available within five to 10 years.

The Light Stuff

MICROPHOTONICS CENTER AIMS TO MAKE OPTICS AS PRACTICAL AS ELECTRONICS

AT A GLANCE

NAME
Microphotonics Center

DIRECTOR
Lionel Kimerling

CONTACT
web.mit.edu/mphotonics/www/

MAJOR PROJECTS
Communications technology road map

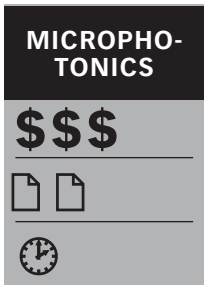
Integrated optical circuits

Photonic crystals

New optical materials

Microprocessors are getting faster all the time, but computers still face a looming bottleneck. The copper wires that carry signals within and between chips are approaching a fundamental limit where they won't be able to carry data any faster. But what if you could take the copper out, and shunt the data around on beams of light?

"You replace an electron with a photon, and now everything moves at the speed of light," says George Kenney, associate director of the MIT Microphotonics Center. Experts estimate the copper bottleneck will be reached this decade, but Kenney says optical interconnects could let computers sprint ahead to a point at which they are capable of, among other things, producing real-time, 3-D holographic images of people talking kilometers apart. Center researchers are pushing toward that vision by trying to develop new optical circuits and new semiconductor and organic materials.



The 10-year-old center, which is located in Building 12 at the heart of the campus, was one of the world's first labs to focus on microphotonics. Now it aims to create a whole new industry. In the last year, center researchers submitted 92 patent disclosures to MIT's technology licensing office, adding to the total of 315 over the five years prior. And it organized the Microphotonics Center Industry Consortium to conduct precompetitive research for companies such as Nortel Networks. Among the startups spinning out of the center is OmniGuide Communications. Founded by John Joannopoulos, Omniguide is developing a type of optical fiber that uses nanoscale photonic crystals to manipulate light—even bending it 180 degrees.

According to director Lionel Kimerling, the goal of the center is to help make photonics as practically applicable as electrical engineering. Right now, Kimerling says, photonics is comparable to "the early days of electronics"—before integrated circuits—when individual components had to be wired together. What the center aims to do, essentially, is invent a photonic integrated circuit that can be cheaply mass produced.

A key stage in the center's quest will be the determination of a material on which to base the new circuit—something comparable to the complementary metal oxide semiconductor (CMOS) form of silicon from which virtually all computer chips are made. Optical devices today are made from a variety of compounds, including gallium arsenide, indium phosphide, and organic materials. Microphotonics researchers, therefore, are looking for ways to integrate these different materials into a single system.

In its effort to lay a technological foundation for optical computing, says Kimerling, the center is teaming with various MIT engineering departments, as well as the Sloan School of Management, to produce a "communications technology road map." This grand plan will outline where the industry is headed and set targets for the development of crucial technologies.(The semiconductor industry is guided by just such a road map.) "The road map has the potential to be very significant to the photonics industry," says Bruce Wallace, director of advanced technology economics at Nortel and a member of the board that oversees the industry consortium. The road map can only be assembled, he says, by combining technical expertise with an understanding of market demand, as MIT is doing. The road map project is headed by Rajeev Ram of the electrical engineering and computer science department and Charles Fine of Sloan.

For example, one near-term milepost on the road map is the development of a low-cost transceiver—a chip that can turn an optical signal into an electrical signal, and vice versa. Such a chip, which the road map has entering the market in 2005, could extend fiber-optic networks into individual homes; a box fitted with such a transceiver would translate the optical signal into electrons a PC or television could use. Getting data as close to its destination as possible in optical form extends the advantages of lightwave transmission's huge bandwidth. Eventually, researchers would like information to travel optically not just from one information appliance to another, but within a single computer chip, vastly speeding up all sorts of devices.

Correction:
The profile of the Center for Cancer Research in the July *MIT Technology Insider* should have said that biologist Luk van Parijs's paper on gene silencing was published in *Nature Genetics*. Also, Nobelist Har Gobind Khorana was an MIT faculty member but not affiliated with the center.

DATEBOOK

September 17-18

Aerospace/Defense—Industry Sector Symposium

Wong Auditorium, Tang Center

ilp.mit.edu/ilp/Conferences/Current.html

September 24-25

The Emerging Technologies Conference at MIT

Kresge Auditorium

www.etc2003.com

October 15-16, 2003

10th Annual Research and Development Conference: Managing R&D as a Global Enterprise

Kresge Auditorium

ilp.mit.edu/ilp/Conferences/Current.html

"Canary" Could Be Gold Mine

A Richmond, VA, startup hopes to use a detection technology developed at MIT to test for pathogens such as anthrax and *E. coli.*

ASD BioSystems, founded in April, has signed an option agreement to license the technology for use in equipment that could detect environmental contaminants or biological agents. The sensor, developed by researchers at MIT Lincoln Laboratory and the MIT Center for Cancer Research, is called Canary, for cellular analysis and notification of antigen risks and yields. It uses B lymphocytes, cells from the human immune system, which have been genetically modified to emit light within seconds of being exposed to specific bacteria and viruses.

ASD plans to incorporate Canary technology into handheld sensors that the company is developing to test biological samples from air, water, or surfaces. "The type of instrument we're designing would be easy to use for people with relatively little lab experience," says ASD president James Tuite.

While the initial market for such devices would be in homeland security—for police, FBI agents, or health officials testing for biological weapons—the larger potential lies in the growing field of biosafety, Tuite says. Companies that work in agriculture, food distribution, and pharmaceuticals want to be assured they don't suffer from dangerous and costly contamination, without having to wait for a lab to return test results, he says. "The ability to get rapid answers to people at the point where they need it, when they need it, will be a high-demand product," he predicts.
www.asdbiosystems.com

RNA Companies Merge

Alnylam Pharmaceuticals has merged with Ribopharma of Kulmbach, Germany, to form a single company working on therapeutic RNA interference. The two companies are developing drugs that interfere with the RNA a cell uses to create proteins. Such interference could be used to shut down the cellular machinery that leads to cancer or reproduces viruses such as HIV.

The merged company, known as Alnylam Holding, will be headquartered in Cambridge, MA, and led by John Maraganore, previously president of Alnylam. The new company has secured $24.6 million in private equity financing from Polaris Venture Partners, Abingworth Management, Cardinal Partners, Atlas Ventures, Arch Venture Partners, and others. That infusion brings Alnylam Holding's total funding to $43 million. Alnylam plans to hire researchers and marketing specialists to speed the development and introduction of new drugs.

Anylam brings to the mix patents for the fundamental technology of RNA interference, while Ribopharma has patents for therapeutic applications. The companies also have a history of collaboration with research leaders in the field, including MIT, the University of Massachusetts Medical Center, the Max Planck Institute in Germany, and Rockefeller University in New York. Alnylam was founded in 2002 by, among others, Phillip Sharp of the MIT Center for Cancer Research and David Bartel of MIT's Whitehead Institute for Biomedical Research. Sharp, a Nobel laureate, will sit on the board.
www.alnylam.com

Magnetic Attraction for Drug Discovery

A patented method for binding nucleic acids to microparticles with magnetic properties—a technique that could be used by biotech and pharmaceutical companies in drug development—has been licensed to Agencourt Bioscience. The patent is owned by MIT's Whitehead Institute for Biomedical Research and joins two other Whitehead patents on techniques for isolating nucleic acids for DNA sequencing and genetic research. "[The patents] all allow one to be able to bind different DNA species to magnetic particles," says Kevin McKernan, Agencourt's co–chief scientific officer. The technology, called solid-phase reversible immobilization, was developed at Whitehead by Trevor Hawkins. McKernan and the other co–chief scientific officer, Paul McEwan, were part of the technology development group for the Human Genome Project at Whitehead. In June 2000, the two cofounded Agencourt, in Beverly, MA, to commercialize some of the sequencing technology they'd come up with.
www.agencourt.com

Financing an Evolutionary Concept

MIT spinoff company Affinova, which employs combinatorial mathematics to mimic evolution in the development of consumer products, has completed a $6 million round of financing. The firm in Cambridge, MA, uses a patent-pending computer program based on concepts from the field of genetics to "evolve" products, packages, and marketing concepts in response to real-time consumer feedback.

The company was cofounded in 2000 by chief technology officer Karnal Malek, formerly on the staff of MIT's Industrial Performance Center, where he compared the strategies and organization of new-product development projects from different countries and industries. Malek also holds bachelor's, master's, and doctoral degrees in mechanical engineering from MIT.

Financing was led by Flagship Ventures, whose senior managing director and CEO is Noubar Afeyan, a senior lecturer at MIT's Sloan School of Management.
www.affinova.com

Companies without Center

SLOAN MANAGEMENT PROFESSOR THOMAS MALONE EXPLAINS HOW TECHNOLOGY CAN DECENTRALIZE COMPANIES AND IMPROVE DECISION-MAKING

> "Information technology is enabling decision-making to be more widely dispersed. And when more people make more of their own decisions, they are more creative, more motivated, more dedicated."

MITTI: Many people are skeptical about the impact of technology on business today. Are there reasons for such skepticism?
Malone: I think many people are still suffering from the post-dot-com-boom hangover and not yet realizing the genuine potential of all these new technologies. Many people overestimated the speed with which these things would happen and were then disillusioned, but I believe that we are about to come out of the disillusionment period. The next few years will be very interesting for people who are thinking about how to take advantage of communications technologies such as e-mail and the Web and the new ways of organizing work they are enabling.

MITTI: What do you think are some of these organizational changes that new technologies are making possible?
Malone: One of the most important things is decentralization. People have talked about this before, but now changes are happening much more radically. Information technology is enabling decision-making to be far more widely dispersed in both large and small firms. With cheaper communication costs, many more people can make decisions for themselves, because they have the information they need. And when more people make more of their own decisions, they are often more creative, more motivated, more dedicated. That means we'll be able to have many of the economic benefits of large organizations without having to give up human benefits of smaller ones—things like motivation, creativity, and freedom.

MITTI: Have you seen these transformations already happening in companies?
Malone: Yes. One example is AES Corp., a big electric-power producer, where there's a huge amount of freedom for people at very low levels in the organization. Junior people can make multi-million-dollar decisions about technology and even business acquisitions, in part because they have the information in their hands and can easily ask advice from people throughout the company. Another example is a company in Spain called Mondragon Cooperatives that gives everyone in the organization a right to vote on who the leaders of the organization will be and other major decisions. So it seems clear to me that lots of companies today are moving away from the rigid, hierarchical ethos that was pervasive in business 20 years ago.

MITTI: How can companies invest smartly in technology in a time of limited budgets?
Malone: I think some of the most interesting uses of technology may not require huge and expensive technology. All they require is creativity. So just because your budgets are limited doesn't mean your creativity should be. For example, there's a huge potential for companies to create knowledge repositories about business processes that let them rapidly consider many different, new ways of doing things. Such systematically structured repositories of knowledge would be very helpful, for instance, in creating Web services and developing whole new applications from components that existed in different places within the company or in other companies all over the Web. This offers promising opportunities, but few companies are taking advantage of it yet.

MITTI: How will new technologies affect the global economy?
Malone: One of the most important constraints on how businesses are organized is the cost of communicating. As that cost plummets, there are many new possibilities. It's becoming almost free to communicate with people anywhere in the world. We're in the early stages of the globalization of the labor market; it's becoming possible to move more and more kinds of jobs to different places in the world and have them be performed just as effectively. My colleague Robert Laubacher and I see the emergence of an "e-lance" economy. "E-lance" stands for electronically connected freelancers. In this world, many of the things that are today done by large corporations could be done by temporary combinations of very small companies, in many cases even individual freelance contractors. Most people don't begin to understand yet how important and how far-reaching this and other decentralization changes will be. They will give us an opportunity to shape the world for the rest of the century.

Thomas Malone is a professor of management at MIT's Sloan School of Management and director of the Center for Coordination Science. He is the editor of Inventing the Organizations of the 21st Century *and* Organizing Business Knowledge, *both to be published by MIT Press in September.*

The "IT" of MIT

Startups that launched between 1999 and 2003 and license information technology from MIT

COMPANY	CONTACT	LAUNCHED OR LICENSED	TECHNOLOGY
AXIOMATIC DESIGN SOFTWARE	221 North Beacon Street Boston MA 02135 www.axiomaticdesign.com	June 1999	Software for deriving, documenting, and optimizing the manufacture of automotive, aerospace, semiconductor, and medical products
FRICTIONLESS COMMERCE	400 Technology Square Cambridge MA 02139-3583 www.frictionless.com	February 1999	Software that helps companies analyze and prioritize how they spend money and identify opportunities to outsource projects
KENET	55 Walkers Brook Drive Reading MA 01867	April 2002	Low-power components for wireless communications
MOCA SYSTEMS	One Gateway Center Suite 808 Newton MA 02458 www.mocasystems.com	March 2000	Simulation software that models the performance of work on a construction site so that the owner, architect, or contractor can assess project cost estimates, schedules, and design and materials options
PEPPERCOIN	41 Academy Street Arlington MA 02476 www.peppercoin.com	April 2001	Payment system that provides an efficient and profitable method for processing small online transactions
PREDICTIVE POWER SERVICES	19 Cypress Street Somerville MA 02143 www.predictivepower.net	July 2001	Proprietary sensors and communications and analysis software to help improve the reliability of power industry equipment
SANDBURST	600 Federal Street Andover MA 01810 www.sandburst.com	July 2000	Chips that streamline communications-protocol processing to eliminate network bottlenecks
STARFESTIVAL	P.O. Box 401025 Cambridge MA 02140-0011 www.starfestival.com	April 1999	Multimedia curriculum that uses CD-ROMs and online programs to teach K-12 schoolchildren about Japan and issues of cultural identity
VRMOTION	Piazza Europa 10 35027 Noventa Padovana Padova, Italy www.vrmotion.com	July 2001	Device for teaching motor skills, both for rehabilitation and to enhance physical performance
WAMIT	822 Boylston Street Suite 202 Chestnut Hill MA 02467-2504 www.wamit.com	October 1999	Software that analyzes the interaction of waves with offshore platforms and seaborne vessels
WEATHER DECISION TECHNOLOGIES	1818 W. Lindsey Avenue Bldg. D Suite 228 Norman OK 73069 www.wdtinc.com	June 2000	System that predicts hazardous weather

SOURCE: MIT Technology Licensing Office